CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Lithium (Perfluoro Octane) Sulfonate

Chemical Code # 5678, Tolerance # 52771
SB 950 # NA

Date: 5/10/00

I. DATA GAP STATUS

Chronic toxicity, rat:	No study on file[1]
Chronic toxicity, dog:	No study on file[1]
Oncogenicity, rat:	No study on file[1]
Oncogenicity, mouse:	No study on file[1]
Reproduction, rat:	No study on file[1]
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 171468 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.
File name: T000510
T. Moore, 5/10/00

[1] New active ingredient, lithium (perfluoro octane) sulfonate, was submitted for terrestrial non-food use. These studies are not required at this time.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

Study not submitted.

CHRONIC TOXICITY, RAT

Study not submitted.

CHRONIC TOXICITY, DOG

Study not submitted.

ONCOGENICITY, RAT

Study not submitted.

ONCOGENICITY, MOUSE

Study not submitted.

REPRODUCTION, RAT

Study not submitted.

TERATOLOGY, RAT

** 030; 171463; "Definitive Teratology Study with Lithium Perfluorooctane Sulfonate, 96% (6861D11) in Rats"; (S.M. Henwood; Hazleton Wisconsin, Inc., Madison, WI; Project ID HWI 6106-108; 5/12/93); Twenty four or 25 mated female Crl:CD rats/group were treated by oral gavage with 0, 3, 6, or 12 mg/kg/day of LPOS (purity: 96%) (lot no. 101) from day 6 through day 15 of gestation. Four of the females in the high dose group were euthanized *in extremis* on gestation days 17 or 19. Another female in that group was found dead on day 18. Clinical signs of hunched posture, recumbency and staining of the anogenital region were noted for the high dose animals. In addition, one of the animals which died displayed tremors and convulsions with rigid and flaccid body tone. Lower mean body weight gain was demonstrated by both the 6 and 12 mg/kg/day groups ($p<0.01$) over the course of the treatment period. Likewise, mean daily food consumption was lower for these two groups during the treatment period ($p<0.01$). In addition, the mean daily food consumption for the 3 mg/kg/day treatment group was lower than that of the control from days 12 to 16 of gestation ($p<0.01$). Late resorptions and fetal death occurred in the high dose group. The mean fetal weight of the 12 mg/kg/day treatment group was lower than that of the control group ($p<0.01$). The high dose group suffered from cleft palate (84/107), and edema (93/259) as well as an increased incidence of unossified bones. **No adverse developmental effect evident. Maternal NOEL:** < 3 mg/kg/day (based upon reduced food consumption by the 3 mg/kg/day group), **Developmental NOEL:** 6 mg/kg/day (based upon lower mean fetal weight and incidence of late resorptions, fetal death, cleft palate and edema in the fetuses of the 12 mg/kg/day treatment group); **Study acceptable**. (Moore, 3/14/00)

TERATOLOGY, RABBIT

** 029; 171462; "Definitive Teratology Study with Lithium Perfluorooctane Sulfonate, 96% (6861D11) in Rabbits"; (S.M. Henwood; Hazleton Wisconsin, Inc., Madison, WI; Project ID. HWI 6106-109; 5/18/93); Sixteen mated female New Zealand White rabbits/group were treated by oral gavage with 0, 1, 2, or 4 mg/kg/day of LPOS (purity: 96%) (lot no. 101) from day 7 through day 19 of gestation. One doe each in the 2 and 4 mg/kg/day treatment groups died. One doe in the 1 mg/kg/day and 3 does in the 4 mg/kg/day aborted their offspring between days 21 and 25 of gestation. Three other females in the high dose group delivered their litters early (days 28 or 29). There was a dose-related decrease in body weight gain over the treatment period (1 mg/kg/day: $p<0.05$; 2 and 4 mg/kg/day, $p<0.01$). The number of does producing few or no feces during the dosing period increased in a treatment-related manner. The number of early and late resorptions suffered by the high dose females was greater than that of the control

animals ($p<0.05$). The 4 mg/kg/day treatment level was toxic to the does based upon the lower mean body weight and the increased incidence of abortion. The mean body weight of the fetuses in the 4 mg/kg/day group was lower than that of the controls ($p<0.01$). In accordance with the lower body weight, skeletal development was retarded with a greater incidence of unossified bones in the high dose offspring. **No adverse developmental effect was evident. Maternal NOEL:**<1 mg/kg/day (based upon the lower body weight gain and decreased fecal production in the 1 mg/kg/day treatment group), **Developmental NOEL:** 2 mg/kg/day (based upon the increased number of resorptions and lower mean fetal weight for the 4 mg/kg/day treatment group); **Study acceptable.** (Moore, 3/13/00)

GENE MUTATION

** 031; 171464; "*Salmonella*/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) with a Confirmatory Assay"; (R.H.C. San and V.O. Wagner; Microbiological Associates, Inc., Rockville, MD; Study No. T9947.501014; 1/8/92); *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were treated for 48 hours at 37° C with LPOS (purity: 96%)(lot no. C8F17503 Li) at concentrations ranging from 100 to 10000 µg/plate with and w/o activation. Two trials were performed. Each treatment level was plated in triplicate. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was no treatment-related increase in the incidence of reverse mutation. **No adverse effect indicated. Study acceptable.** (Moore, 3/15/00)

** 032; 171465; "CHO/HGPRT Mutation Assay with Confirmation"; (C.A. H. Bigger and C.I. Sigler; Microbiological Associates, Inc., Rockville, MD; Study No. T9947.332001; 6/4/92); Chinese Hamster Ovary (CHO-K_1-BH_4) cells were treated with LPOS (purity: 96%) (6861D11) (lot no. C8F17503 Li) for 5 hours at 37° C with and w/o activation. Three and four trials were performed under non-activated and activated conditions, respectively with duplicate samples for each treatment level. In the non-activated trials, treatment levels ranged between 900 and 4000 µg/ml (trial 1), 1000 and 2500 µg/ml (trial 2) and 1000 and 2750 µg/ml (trial 3). In the activated trials, treatment levels ranged from 750 to 1500 µg/ml (trial 1), 150 to 1500 µg/ml (trial 2), and 1000 to 1600 µg/ml (trial 3 and 4). An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was no apparent treatment-related increase in forward mutation rate. **No adverse effect indicated. Study acceptable**. (Moore, 3/17/00)

CHROMOSOME EFFECTS

** 033; 171466; "Micronucleus Cytogenetic Assay in Mice"; (D.L. Putnam and R.R. Young; Microbiological Associates, Inc., Rockville, MD; Study No. T9947.122; 4/10/92); Five ICR mice/sex/group/time point were treated ip with 0 (water), 24, 48 or 95 mg/kg of LPOS (purity: 96%) (6861D11) (lot no. C8F17503 Li) and euthanized at 24, 48 or 72 hours after dosing. An additional 5 animals/sex were treated with the positive control (cyclophosphamide, 30 mg/kg) and euthanized 24 hours after dosing. Bone marrow samples from the femur were examined. The percentage of PCE with micronucleus and ratio of polychromatic erythrocytes (PCE) to the total number of erythrocytes were determined. No treatment-related increase in the number of PCE with a micronucleus was noted. **No adverse effect indicated. Study acceptable.** (Moore, 3/17/00)

034; 171467; "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells"; (D.L. Putnam and M.J. Morris; Microbiological Associates, Inc., Rockville, MD; Study No. T9947.337; 1/6/92); Chinese Hamster ovary cells (CHO-K_1), (CCL 61) were exposed to LPOS (purity: 96%) (lot no. C8 F17503 Li) at concentrations ranging from 350 to 1400 µg/ml under conditions of both non-activation and activation. Non-activated samples were treated for 10 hours. The activated samples were treated for 2 hours, washed, and incubated for an additional 8 hours. In both assays, the cells were incubated for an additional 2 hours in the presence of Colcemid prior to fixation. All of the incubations were performed at 37° C with duplicate cultures at each treatment level. In the non-activated samples, there was an apparent dose-related increase in the percentage of aberrant cells. Although this percentage did not achieve statistical significance at the highest treatment level, the value approached that of the positive control. A second trial should have been performed in order to establish whether this increase was treatment-related. **Presence or absence of adverse effect not determinable. Study unacceptable, not upgradeable**.

(Moore, 3/28/00)

DNA DAMAGE

** 035; 171468; "Unscheduled DNA Synthesis in Rat Primary Hepatocytes"; (R.H.C. San and H.A. Raabe; Microbiological Associates, Inc., Rockville, MD; Study No. T9947.380; 5/5/92); Primary rat hepatocyte cultures were exposed to LPOS (purity: 96%) (lot no. C8F17503Li) at concentrations ranging from 1.5 to 500 µg/ml for 18 to 20 hours at 37° C. Vehicle and positive (DMBA, 10 µl/ml) controls were included in the assay. There were 3 cultures/treatment level. There was no treatment-related increase in unscheduled DNA synthesis. **No adverse effect indicated. Study acceptable.** (Moore, 3/28/00)

NEUROTOXICITY

Study not submitted.

SUBCHRONIC STUDIES

52771-028; 171461; "Ninety (90) Day Subchronic Oral Toxicity Study of Lithium Perfluorooctane Sulfonate in Drinking Water in Sprague Dawley Rats"; (J. Limoges; Biological Test Center, Irvine, CA; Study No. P0493001; 6/27/95); Ten male rats/group were dosed orally in the drinking water with 0, 0.3, 1.0 or 3.0 mg/kg/day of LPOS (lot no. 101; purity: 96.87%) for 90 days. Ten female rats/group were likewise treated with 0, 0.02, 0.06 or 0.20 mg/kg/day of the test material for 90 days. When the high dose females failed to demonstrate any treatment-related effects, an additional study was instituted with ten females/group treated with 0 or 0.60 mg/kg/day of the test material for 91 days. No mortality nor clinical signs resulted from the treatment. The mean body weights for the respective high dose male and female groups were 87.5 ($p<0.05$) and 90.6% of those of the control after 13 weeks of treatment. Mean values for red blood cell counts, hemoglobin and hematocrit for the males were affected in a dose-related manner with lower mean values noted for both 1.0 and 3.0 mg/kg/day groups ($p<0.05$). Similarly, the mean rbc count and hematocrit were lower for the females at 0.6 mg/kg/day ($p<0.05$). For the males, mean serum total bilirubin was elevated in the 3.0 mg/kg/day group ($p<0.05$). In contrast, the mean serum cholesterol and triglyceride levels were decreased in a dose-related manner, with significance ($p<0.05$) noted for cholesterol in the 1.0 mg/kg/day group and triglycerides in the 0.3 mg/kg/day group. The mean blood urea nitrogen was increased in the 1.0 and 3.0 mg/kg/day groups ($p<0.05$). The mean absolute liver and relative liver weights were increased in a treatment-related manner with significance ($p<0.05$) noted for the 1.0 and 3.0 mg/kg/day groups. The mean relative kidney and testes weights were increased in the 3.0 mg/kg/day group. Histopathologic examination of the livers in the 3.0 mg/kg/day treatment group revealed an increased incidence and severity of hepatocytic vacuolation. Target Organ: liver and blood parameters. **No adverse effect indicated. NOEL:** (M) <0.3 mg/kg/day (based upon the reduction of serum triglycerides in the 0.3 mg/kg/day treatment group), (F) 0.2 mg/kg/day (based upon the lower rbc count and hematocrit and greater mean liver weight in the 0.6 mg/kg/day treatment group); **Study acceptable.** (Moore, 3/9/00)